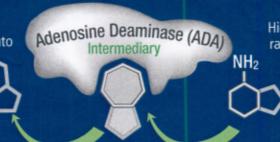
Nipent®

The distinctive purine analog with a unique mechanism of action.

ADA catalyzes conversion of deoxyadenosine and adenosine into deoxyinosine and inosine.¹²



High ADA activity characterizes rapidly proliferating T cells and B-cell malignancies.\(^2\)

Unlike most purine analogs, Nipent tightly binds to and inhibits ADA, the enzyme essential for purine metabolism.

NH2

Nipent prevents the enzymatic action of ADA by competitively blocking its intermediary's activation site! Inhibiting ADA increases intracellular accumulation of deoxyadenosine and adenosine.^{1,2}

Adenosine buildup potentiates TNF inhibition.

Accumulated deoxyadenosine is phosphorylated into dATP.²

dATP inhibition of RR causes a relative deficiency of other dNTPs.

> dNTP deficiency causes DNA breaks to appear.²

Unrepaired breaks cause DNA synthesis to fail.12

KEY

ADA = adenosine deaminase dATP = deoxyadenosine triphosphate RR = ribonuclease reductase TNF = tumor necrosis factor dNTP = deoxynucleotide triphosphate

Deteriorating DNA repairmechanisms lead to cell death.

Nipent is selectively cytotoxic to the leukemic population, exhibiting little or no effect on stem cells:

Through selective, potent, and strong ADA inhibition, Nipent retards DNA repair mechanisms and induces apoptosis while inhibiting TNF.

Nipent is indicated as first-line treatment for hairy cell leukemia.



SuperGen, Inc. 4140 Dublin Boulevard, Suite 200 Dublin, CA 94568

References

1. Kane BJ, Kuhn JG, Roush MK. Pentostatin: an adenosine deaminase inhibitor for the treatment of hairy cell leukemia. Ann Pharmacother. 1992;26:939-947. 2. Chu E, Mota AC, Fogarasi MC. Antimetabolites. In: DeVita VT Jr, Hellman S, Rosenberg SA, eds. Cancer Principles & Practice of Oncology. 6th ed. Philadelphia, PA: Uppincott Williams & Wilkins; 2001:388-415. 3. Le Moine O, Quertinmont E, Gulbis B, Devière J. Blunted anti-inflammatory response to adenosine in alcoholic cirrhosis. J Hepatol. 1999;31:457-463. 4. Aye MT, Dunne JV. Effect of 2'-deoxycoformycin on erythroid, granulocytic, and T-lymphocyte colony growth. Blood. 1981;58:1043-1046.

Nipent*
Pentostatin for Injection



The distinctive purine analog with a unique mechanism of action.

ADA catalyzes conversion of deoxyadenosine and adenosine into deoxyinosine and inosine.1.2



High ADA activity characterizes rapidly proliferating T cells and B-cell malignancies.12

Unlike most purine analogs, Nipent tightly binds to and inhibits ADA, the enzyme essential for purine metabolism.

NH2

Nipent

Apoptotic Ce

Nipent prevents the enzymatic action of ADA by competitively blocking its intermediary's activation site.

Inhibiting ADA increases intracellular accumulation Adenosine Deaminase (ADA) of deoxyadenosine and adenosine.1.2

> Adenosine buildup potentiates TNF inhibition.3

Accumulated deoxyadenosine is phosphorylated into dATP.2

> dATP inhibition of RR causes a relative deficiency of other dNTPs.1

> > dNTP deficiency causes DNA breaks to appear.2

Unrepaired breaks cause DNA synthesis to fail.12

ADA = adenosine deaminase

dATP = deoxyadenosine triphosphate

RR = ribonuclease reductase

TNF = tumor necrosis factor

dNTP = deoxynucleotide triphosphate

Deteriorating DNA repairmechanisms lead to cell death. Nipent is selectively cytotoxic to the leukemic population, exhibiting little or no effect on stem cells.

> Through selective, potent, and strong ADA inhibition, Nipent retards DNA repair mechanisms and induces apoptosis while inhibiting TNF.

Nipent is indicated as first-line treatment for hairy cell leukemia.

Please see full prescribing information, including boxed warning, on back.

1. Kane BJ, Kuhn JG, Roush MK. Pentostatin: an adenosine deaminase inhibitor for the treatment of hairy cell leukemia. Ann Pharmacother. 1992;26:939-947. 2. Chu E, Mota AC, Fogarasi MC. Antimetabolites. In: DeVita VT Jr, Hellman S, Rosenberg SA, eds. Cancer Principles & Practice of Oncology. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:388-415. 3. Le Moine O, Quertinmont E, Gulbis B, Devière J. Blunted anti-inflammatory response to adenosine in alcoholic cirrhosis. J Hepatol. 1999;31:457-463. 4. Aye MT, Dunne JV. Effect of 2'deoxycoformycin on erythroid, granulocytic, and T-lymphocyte colony growth. Blood. 1981;58:1043-1046.

Nipen Pentostatin for Injection



SuperGen